REMARKS/ARGUMENTS

I. Status

The specification was amended to correct a typographical error.

The subject matter of claim 30 was incorporated into claims 1 and 2. Accordingly, claim 30 was cancelled and claim 31 was amended to depend from claim 1 instead of claim 30.

New claim 38 recites a coiled capillary device having a bend radius of less than 2 cm. Support for new claim 38 can be found for example, in Applicant's specification on page 53, lines 22 - 31.

The amendments are fully supported by the application as filed and do not introduce new matter. Entry of these amendments is respectfully requested.

II. Election/Restriction

Applicants acknowledge the maintenance of the restriction requirement.

III. Claim Rejections under 35 U.S.C. §103

A. Xiao et al. in view of Haase and further in view of Le Febre et al.

Claims 1 and 2 were amended herein to include the subject matter of claim 30, coiled capillaries having a bend radius of less than 3 cm. All claims pending in the instant application depend from claims 1 or 2, so all claims are limited to capillaries having a bend radius of less than 3 cm. On page 5 of the Office action, the Examiner rejected claim 30 as allegedly unpatentable over Xiao et al. ("Xiao", US 20020164824) in view of Haase ("Haase", US 5,276,062) as applied to claims 1, 2, 7-9, 11, 34 and 35 and further in view of Le Febre et al. ("Le Febre", US 5,552,042). The Examiner states, "Neither Xiao et al. nor Haase disclose the bend radium of the capillary." Therefore, Le Febre et al. is the sole reference relied upon by the Examiner to teach a bend radius of less than 3 cm.

The Examiner states, "Le Febre et al disclose a coiled capillary wherein the diameter of the coil ranges from 50 microns to 10 inches. In light of the disclosure of Le Febre et al., it would have been obvious to one of ordinary skill in the art to form the capillary of the modified Xiao et al. apparatus into a coil having a diameter of less than 3 cm if a coil having a diameter of less than 3 cm is desired." Applicants respectfully traverse the rejection on the basis that (1) Le Febre does not in

fact, teach a bend radius of less than 3 cm and (2) Le Febre actually teaches away from a bend radius of less than 3 cm.

Le Febre's terminology

On page 5 of the Office action, the Examiner alleges that Le Febre discloses a coiled capillary wherein the diameter of the coil ranges from 50 microns to 10 inches. It appears that the Examiner's allegation that Le Febre teaches a diameter of the coil as small as 50 microns stems from a misunderstanding of Le Febre's terminology. The section of Le Febre cited by the Examiner is reproduced here for the purposes of discussion.

> The purpose of this invention is the preparation of a relatively stress free, rigid capillary or open tubular assembly not requiring a protective coating while stable to operation at high temperature, and stable to repeated temperature cycling for long periods of time. One embodiment is a helical coil of a hollow silica tube wound on the outside of a hollow mandrel of a material of similar coefficient of expansion. The coils are in contact with the mandrel along substantially the entire length of the coils and are fused to the mandrel at substantially all contact points. In a more specific embodiment the mandrel is silica. In yet another embodiment the **mandrel has a diameter** between about 3 and about 10 inches. In still another specific embodiment the **inside diameter of the tubular coil** ranges from about 50 microns up to about 5 mm. (Emphasis added)

A careful reading of the above section reveals two different dimensions of Le Febre's coiled capillary: a **mandrel diameter of 3 to 10 inches** and an **inside diameter of the tubular coil** ranging from **50 microns to 5 mm**. Applicants submit that Le Febre's "mandrel diameter" is the term relevant for comparison to Applicant's "coil diameter".

It is important to keep in mind the relationship between the radius and the diameter of a circle. The diameter of a circle is twice the radius. Applicant's specification describes the relationship between coil diameter and bend radius as follows. "In the case of a coil, for example, a coil diameter of 2 cms corresponds to a bend radius of 1 cm.[1]" Applicant's specification defines the

[1] Applicant's specification, page 54, lines 1 – 2.

term "bend radius" as the radius of a bend in the capillary tubing[2]. Therefore, Le Febre's "mandrel radius" corresponds to Applicant's "bend radius". It follows that 3-inch lower limit of the mandrel diameter taught by Le Febre teaches a mandrel radius of 1.5 inches. In contrast, Applicant's amended claims recite a bend radius of less than 3 cm.

Le Febre does not teach a capillary having a bend radius of 50 microns.

Although the Examiner alleges, "Le Febre et al disclose a coiled capillary wherein the diameter of the coil ranges from 50 microns…" this is not the case. Le Febre teaches an **inside diameter of the tubular coil** ranging from 50 microns to 5 mm. The term, "**inside diameter of the tubular coil"** refers to the inner diameter of the capillary tubing, not the diameter of the coils.

A bend radius of 50 microns goes against common sense. A sheet of paper is roughly 100 microns thick. Therefore, a capillary having a coil diameter of 50 microns would have a coil diameter of half the width of a sheet of paper, which is not even physically feasible.

Furthermore, Le Febre teaches a device used for gas chromatography. In column 3, Le Febre describes a mandrel diameter of about 3 to 10 inches and preferably about 5 to 7 inches. Le Febre goes on to state, ["… the foregoing diameters represent practical limitations arising largely from the chromatographic instruments presently commercially available". Applicants submit a person of ordinary skill in the art of gas chromatography knows there are no commercial gas chromatographs available with a coil radius of 50 microns.

A bend radius of less than 3 cm is not obvious.

First, according to section 2145 of the MPEP, proceeding contrary to accepted wisdom in the art is evidence of non-obviousness. It is Applicant's position that the claimed capillaries having a bend radius of less than 3 cm are contrary to accepted wisdom in the art. Second, section 2141.02 of the MPEP states, "A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention.[3]" The references discussed below (including Le Febre et al. cited by the Examiner) teach away from the claimed invention. Finally, section 716.02 of the MPEP states, "Presence of a property not possessed by the

[2] Applicant's specification, page 53, line 31 through page 54, line 1.
[3] W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), cert. denied, 469 U.S. 851 (1984)

prior art is evidence of nonobviousness.[4]" Applicants submit that capillaries having a bend radius of less than 3 cm is a property not possessed by the prior art.

a. Le Febre

Le Febre actually teaches away from the coil bend radius of less than 3 cm of the claimed invention. Le Febre describes a problem in the field of gas chromatography that glass capillary columns configured in helical coils had the serious disadvantage of being fragile, inflexible and susceptible to stress fracture[5]. To solve these problems, Le Febre anneals or fuses a coiled open tubular capillary assembly to the outside of a hollow mandrel. The coiled capillary is fused to the mandrel at substantially all contact points[6]. The fact that Le Febre solves the fragility problem by annealing the entire capillary teaches away from the claimed invention. Even at the large bend diameter of 3 to 10 inches, it was necessary for Le Febre to fuse the capillary to a mandrel to prevent breakage of the coiled capillaries.

b. Polymicro Technologies

Polymicro Technologies, a leading supplier of fused silica capillary tubing, also teach away from the tight coiling of fused silica capillaries. In their book, "The Book on the Technologies of Polymicro", (copyright 2002), Polymicro recommends against tight coiling. Polymicro provides a table of Applied Bending Stress, measured in kpsi for fused silica capillary tubing. Applicants included this table as Figure 22 of their specification. The table (which is inserted below in section c2) gives applied bending stress as a function of bend radius (mm) and total outer diameter (μm). According to Polymicro Technologies, a kpsi of over 100 exceeds capillary break strength and is not recommended.

In Example 51 from Applicant's specification, a capillary having an outer diameter of 360 μm was coiled inside a plastic ring having an inside diameter of 0.55 inches (approximately 1.4 cm). This corresponds to a bend radius of 0.7 cm (7 mm). According to Polymicro Technologies, these capillaries had a kpsi of between 170 and 213, a value well exceeding the recommended 100 kpsi. Therefore, the bend radius of the coiled capillaries used successfully by Applicants in Example

[4] In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)
[5] Le Febre, column 1, lines 16 – 29.
[6] Le Febre, column 2, lines 25 – 40.

51 was recommended against by Polymicro. Therefore, Polymicro Technologies teaches away from the claimed invention.

c. Applicant's specification

Throughout the specification, Applicants repeatedly make reference to the fact that the tight coiling of capillaries is against conventional wisdom.

1. The following passage from Applicant's specification describes the long-held belief that tight coils of fused silica capillary tubing are not recommended due to the bending stress[7].

> While the instant disclosure identifies a number of advantages resulting from the use of the tightly coiled fused silica extraction capillaries, there is a limit to how tightly a fused silica capillary can be coiled or bent without resulting in breakage or other impairment of function. This is because bending the capillary tubing results in applied bending stress in the tubing which will eventually cause the tubing to break if the bending radius is too tight. In an extreme case where the bending radius is very small, breakage occurs at the time of bending. However, at less extreme bending radii the tubing does not initially break, but over the course of time the bending stress will result in a breakdown of the capillary that will impact performance. Thus, although it has been recognized that fused silica capillary tubing can be bent to some degree, e.g., in loose, high bend radius loops, it has been thought that this type of tubing should not be wound into tighter coils of lower bend radius because this would presumably result in an applied bending stress exceeding the capillary break strength. This perceived inability to tightly coil fused silica capillary tubing would dissuade those of skill in the art from attempting to construct some of the compact extraction capillary devices of the present invention. However, the instant inventors have discovered that fused silica capillary tubing can be coiled substantially tighter that previously believed, while retaining the ability to function as an extraction device for

[7] Applicant's specification, page 55, lines 1 – 23.

extended periods of times. By employing these tightly coiled capillaries it is possible to create compact, tightly coiled extraction capillaries for use in extraction devices of the invention that are stable for extended periods.

2. Applicant's specification refers to the applied bending stress table published by Polymicro Technologies and includes their table as Figure 22 (see below).

Applied Bending Stress (kpsi)

	Bend Radius (mm)															
Total OD (μm)	4	6	8	10	15	20	25	30	40	50	60	80	100	130	160	200
90	87	58	43	35	23	17	14	12	9	7	6	4	3	3	2	2
105	106	71	53	43	28	21	17	14	11	9	7	5	4	3	3	2
150	165	110	83	66	44	33	26	22	17	13	11	8	7	5	4	3
164	184	123	92	74	49	37	29	25	18	15	12	9	7	6	5	4
238	270	180	135	108	72	54	43	36	27	22	18	14	11	8	7	5
340	399	266	200	160	106	80	64	53	40	32	27	20	16	12	10	8
360	425	284	213	170	113	85	68	57	43	34	28	21	17	13	11	9
363	424	283	212	170	113	85	68	57	42	34	28	21	17	13	11	8
435	524	349	262	209	140	105	84	70	52	42	35	26	21	16	13	10
665	*	540	405	324	216	162	130	108	81	65	54	40	32	25	20	16
700	*	571	428	342	228	171	137	114	86	68	57	43	34	26	21	17
850	*	*	526	421	281	211	168	140	105	84	70	53	42	32	26	21

FIG.–22

3. Because of the technical obstacles encountered when producing tightly coiled capillaries, Applicant's specification describes special methods requiring great care for coiling the capillaries without the introduction of nicks or other breakage[8]. These methods include:

- Avoidance of twisting while coiling the capillaries
- Use of a thick capillary coating, preferably polyimide
- Minimal exposure to high pH conditions
- Comparison of capillary coiling ability between vendors

[8] Applicant's specification, pages 58, line 23 through page 59, line 27.

- Pre-testing the coilability of particular lots or sections of tubing

d. Kasicka et al.

Kasicka et al. ("Kasicka") teach away from the claimed invention. This reference, which was cited in the IDS for the instant application, quantitatively investigates the influence of capillary coiling on separation efficiency in capillary zone electrophoresis[9]. Kasicka concluded that it is preferred to perform capillary zone electrophoresis in straight, rather than coiled capillaries. Kasicka further concluded that due to the low diffusion coefficients, the separation efficiency in coiled capillaries is negatively impacted to a greater extent for large bioparticles, such as Tobacco Mosaic Virus than for very small analytes such a glycine. However, even for the analysis of glycine, these authors recommend a bend radius greater than 30 mm (3 cm). In contrast to Kasicka, it is hypothesized in Applicant's specification that coils actually help large molecules having a smaller diffusion coefficients travel to the wall of the open tubular capillary.

In summary, multiple references (including Le Febre cited by the Examiner) teach away from the claimed invention. Additionally, capillaries having a bend radius of less than 3 cm is contrary to accepted wisdom in the art. In view of the foregoing, the withdrawal of the § 103 rejection is respectfully requested.

B. Kumar et al. and Smith et al.

Claims 1 and 2 were amended herein to recite coiled capillaries having a bend radius of less than 3 cm. On page 5 of the Office action, the Examiner states that neither Xiao nor Haase disclose a bend radius of their capillaries. Therefore, the Examiner is relying on the Le Febre reference to supply the bend radius of less than 3 cm. However, as Applicants argued above (in section A), the claimed invention is not obvious over Le Febre because Le Febre fails to teach a coiled capillary having a bend radius of less that 3 cm and additionally, Le Febre actually teaches away from coiled capillaries having a bend radius of less than 3 cm.

Kumar and Smith do not supply the missing teachings. Neither Kumar nor Smith teach coiled capillaries having a bend radius of less than 3 cm. Kumar teaches a device for performing immunoassays in one or more capillary tubes. Kumar does not teach coiled capillaries.

[9] Electrophoresis 1995. volume 16, pp 2034 – 2038.

Kumar's capillaries are relatively short in length, typically between 1 and 15 cm[10]. The maximum length of Kumar's capillaries is 25 cm so coiling is not particularly advantageous for Kumar. Smith teaches a process for separating biologically active polypeptides or proteins in packed columns using a resin containing immobilized metal ions. Smith does not teach coiled fused silica capillaries.

[10] Kumar, column 14, lines 19 - 23.

CONCLUSION

Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

The Commissioner is hereby authorized to charge $65 for a one-month extension of time to Deposit Account No. 50-2852. In the event that an extension of time is required in addition to that requested in the enclosed petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 50-2852.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (408)267-7214.

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